UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,456	12/28/2000	Glenn Friedrich	LEX-0286-USA	6630

7590 04/13/2004

Lance K. Ishimoto
Lexicon Genetics Incorporated
4000 Research Forest Drive
The Woodlands, TX 77381

EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/750,456	FRIEDRICH ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 26, 2004 has been entered. Claims 1 and 7 have been amended. Claims 2-6 have been cancelled. The remarks filed September 12, 2003 (hereinafter referred to as "the response") are considered herein.

Claims 1 and 7 remain pending in the instant application.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the **first sentence** of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Although the specification contains a reference to the prior applications it does not specify the relationship between the nonprovisional applications.

Applicants have not addressed this deficiency.

At page 1 of the response, Applicants state that the patent and applications listed in the **second sentence** of the specification are not being relied upon for priority. Nevertheless, the **first sentence** of the specification clearly and unambiguously claims priority to two earlier-filed applications. The specific reference must include the relationship between the applications.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 7 stand rejected under 35 U.S.C. 101, for reasons of record set forth on pages 2-4 of the Office Action mailed 4/8/03 and as further discussed herein below, because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claim 1 is drawn to a genetically engineered mammalian cell that has been mutated by a process comprising the insertion of a recombinantly manipulated polynucleotide sequence into a gene in said genetically engineered mammalian cell wherein said gene is identifiable as corresponding to SEQ ID NO: 393. Claim 7 is drawn to an isolated murine embryonic stem cell line comprising an engineered retroviral gene trap vector in at least one gene comprising a polynucleotide sequence identifiable as encoding SEQ ID NO: 393.

The specification discloses that the claimed cells can be used to produce mutant animals capable of germline transmission of the mutated gene (page 1, lines 23-26). The specification further discloses that the mutated cells and animals are used to investigate and define the cellular and biological functions of the mutated gene (page 13, lines 17-19). However, neither the specification as-filed nor any art of record discloses or suggests any specific property for the cells or the animals that would be produced from the mutated cells such that a utility would be well-established for the cells. Furthermore the specification does not teach a specific asserted utility for the mutated cells because any mutant ES cell can be used to produce mutant animals and therefore this does not constitute a **specific** utility for cells carrying the particular mutation recited in the claims. A **specific** utility is one that is specific to the subject matter claimed. This contrasts with a **general** utility that would be applicable to the broad class of the invention. The contemplated uses of the animals that would be generated from the mutant cells is unspecified. The disclosure generally contemplates that the mutated cells or animals could be used as disease models or in assays for compounds or genes that compensate for the mutant phenotype and which can then be used to treat diseases and disorders related to the observed phenotype (page 15, lines 1-6). However, the disclosure does not specify the mutant phenotype or any specific disease that would be

modelled by the cells or animals. Thus, the asserted utility to use the mutated cells to produce mutant animals as disease models lacks specificity. Moreover, with regard to using the cells or animals produced from the cells to investigate and define the cellular and biological functions of the mutated gene, use of a product to further study the product itself does not define a "real world" context of use and thus does not represent a specific and substantial asserted utility. The utility of generally using the mutated cells or animals produced from the cells to investigate the function of the mutated gene does not define a "real world" context of use but would require or constitute further research to reasonably identify or confirm such a context of use. A utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility. The research contemplated is unspecified. Thus, the asserted utility to study gene function lacks specificity.

Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility cannot be assessed.

At page 2 of the response, Applicants argue that the mutated ES cells claimed have a **specific** utility because they are useful for discovering the function of a **specific** gene. First, a **specific utility** must be contrasted with a **general utility** that would be applicable to the broad class of the invention. In the instant case, the broad class of the invention relates to a murine ES cell having a disrupted gene. Any murine ES cell having a disrupted gene can be used to make a knockout mouse, which can then be used to study the function of the disrupted gene. Thus, such a utility does not constitute a **specific** utility because it is not specific to the gene being disrupted. Second, discovering the function of a gene is not a **substantial** utility because research is not a real world context of use. A substantial utility is one that defines a real world use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a real world context of use are not **substantial** utilities. Basic research, such as studying the properties of the claimed product itself or the mechanisms in which the material is involved, constitutes further research carried out to identify or reasonably confirm a real world context of use.

Likewise, using the claimed product to make a second product, such as a knockout mouse, for the purpose of studying the second product also constitutes further research and therefore does not define a **substantial** utility.

At page 3 of the response, Applicants argue that the mutated ES cell clones are each specifically identified by corresponding exon sequences that provide a unique and specific resource for mapping that portion of the murine genome that encodes the described exon sequence. Applicants further argue that the ES cells can be used to generate animals that specifically lack the function of the disrupted gene and that these animals provide a novel resource for specifically determining the physiological role of the mutated gene. This argument has already been addressed herein above.

At page 4 of the response, Applicants assert that "[g]enetically engineered mice made using the methods referenced in the specification using ES cell clones having mutations in the murine ortholog of the neurexin II gene displayed enhanced sensorimotor gating/attention in conjunction with reduced coordination (optic disc abnormalities were also noted)." Applicants further assert that "by using the specifically described mutated ES cells and following the teaching in the specification, employees of the Assignee of the present application were able to first determine the role of the neurexin II gene in the broader context of mammalian physiology." Applicants assert that the neurexin II protein is an overt target for the development of neurological agents. Applicants further assert that "there can be no question that the 'final product' of the claimed invention has already been used to identify a substantial pharmaceutical utility. Applicants argue that the present invention has shown that the neurexin II protein is one of the relatively small number of proteins that have been shown to have pharmaceutical relevance. Applicants conclude that there can be no question that the claimed ES cell line has a credible, substantial, and specific "real world" utility. First, genetically engineered mice having the phenotype referred to above are not disclosed in the specification. Second, "the role of the neurexin II gene in the broader context of mammalian physiology" is also not disclosed in the specification. Third, nothing in the

specification points to murine neurexin II protein as "an overt target for the development of neurological agents." Fourth, neither the actual nor even the desired activity of such "neurological agents" is disclosed in the specification. It is well established in our law that sufficiency of disclosure under first paragraph of 35 U.S.C. 112 must be judged as of the filing date. If a disclosure is insufficient as of the time it is filed, it cannot be made sufficient, while application is pending, by later information which adds to the knowledge of the art. *In re Glass*, 181 USPQ 31 (CCPA 1974).

At page 5 of the response, Applicants argue that the mouse ES cell clones provide a specific resource for discovering the *in vivo* function of a specific human ortholog. Applicants assert that when these ES cells were used as described in the specification to generate knockout animals, the medical potential of the neurexin II product, as a target for antagonism by a drug, was discovered. These arguments have already been addressed hereinabove. Studying the *in vivo* function of a gene does not represent a **specific** and **substantial** utility, as it is not specific to the gene being studied and does not define a real world context of use.

At pages 5-8 of the response, Applicants argue that the scientific community has accepted the value of knockout mice for discovering the function of genomic sequence information. Applicants cite an awards presentation praising the use of knockout mice for *in vivo* genetic analysis. While *in vivo* genetic analysis is an important methodology for the scientific community, it nevertheless does not represent a real world context of use, but rather constitutes further reasearch for identifying a potential real world context of use.

While the claims are directed to genetically engineered mammalian cells, Applicants arguments are limited to the utility of mouse ES cells. However, the claims cover all mammalian cells, including human, pig, goat, etc., as well as any cell type, including neurons, lymphocytes, astrocytes, etc. One of skill in the art would readily recognize that one cannot use a human cell to make a knockout mouse.

Thus, Applicants' arguments do not apply to any cell type other than mouse ES cells. Therefore, Applicants' arguments are not commensurate in scope with the scope of the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 7 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

At page 10 of the response, Applicants argue that they have shown that the 'final product' of the claimed invention has a real world pharmaceutical utility. This argument has already been addressed herein above. The specification does not disclose a "final product" that has a real world pharmaceutical utility. Thus, one of skill in the art would not know how to use the claimed cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 7 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 remains indefinite in its recitation of "wherein said gene is identifiable as corresponding to SEQ ID NO: 393" because it is unclear what would constitute a gene "corresponding to" SEQ ID NO: 393.

At page 10 of the response, Applicants assert that those skilled in the art would understand that SEQ ID NO: 393 represents exon sequence that is naturally encoded and expressed by the neurexin II locus. Applicants further assert that one skilled in the art would understand that the neurexin II gene corresponds to SEQ ID NO: 393. The question is: What else "corresponds to SEQ ID NO: 393"? The metes and bounds of the claim are not clearly set forth.

Claim 7 remains indefinite in its recitation of "encoding SEQ ID NO: 393" because SEQ ID NO: 393 is a DNA nucleotide sequence, not an amino acid sequence, and therefore the polynucleotide sequence can not "encode" SEQ ID NO: 393.

At page 11 of the response, Applicants assert that genes encode exons. Applicants further assert that those skilled in the art would have little doubt that SEQ ID NO: 393 represents spliced exon sequence. However, the instant specification does not describe a "gene comprising a polynucleotide sequence identifiable as encoding SEQ ID NO: 393." If genes encode exons, then what encodes SEQ ID NO: 393?

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to William Phillips, whose telephone number is (571) 272-0548.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER